# EU Official Control Authority Batch Release

## Human Vaccines

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# Guideline for Pandemic COVID-19 Vaccine (mRNA)

**This version in force from 01/01/2024**
**Replacing version in force from 15/09/2022**

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| **Document title** | Official Control Authority Batch Release Of Pandemic COVID-19 Vaccine (mRNA) |
| **Legislative basis** | Council Directive 2001/83/EC formerly 89/342/EEC, amended by Directive 2004/27/EC |
| **Date of entry into force of present version** | 01 January 2024 |
| **Adoption of present version** | December 2023 |
| **Revision status** | Update to section 3 to align with marketing authorisation dossiers |
| **Previous titles and other references** | Formerly finalised under PA/PH/OMCL (22) 86 DEF |
| **Custodian organisation** | The present document was elaborated by the EDQM in the OMCL network and finalised under PA/PH/OMCL (23) 97 DEF |

# OFFICIAL CONTROL AUTHORITY BATCH RELEASE OF PANDEMIC COVID-19 VACCINE (mRNA)

## 1. Introduction

Control Authority Batch Release of immunological medicinal products is performed within the framework of Article 114 paragraph 1 of Directive 2001/83/EC and Article 1 paragraph 78 of the amending Directive 2004/27/EC and following the current guideline on EC administrative procedure for Official Control Authority Batch Release.

All general and specific Ph Eur monographs pertaining to this product apply.

## 2. Sampling and tests to be performed by the Control Laboratory

The following samples should be supplied to the Official Medicines Control Laboratory performing batch release:

At least 15 single/multi dose containers of each final lot

The Control Laboratory should perform the following tests:

On the final lot:

- Appearance
- Identity (for each strain)
- Integrity

*(if more than one strain, content/ratio of each is measured according to MA)

## 3. Protocol submission

The protocol submitted by the manufacturer should reflect all appropriate production steps and controls for a particular product as outlined in the Marketing Authorisation for that specific product. A **MODEL** protocol is given below to help ensure complete and harmonised protocol submission. An attempt has been made to list all appropriate production steps and controls as required by the various Marketing Authorisations and the relevant monograph(s) of the Ph Eur for products of this type. The manufacturer should omit listed items that are not required by his Marketing Authorisation and include any relevant additional items. It is thus possible that **a protocol for a specific product may differ in detail from the model provided**. The essential point is that **all relevant details demonstrating compliance with the Marketing Authorisation and the Ph Eur monograph(s) (if available) for a particular product should be given in the protocol submitted**.

Results of the tests are required (passed or failed is not sufficient, initial results and, where applicable, results of retests should be given). Sufficient detail should be supplied to allow recalculation of test values. Specifications for each test and dates when the tests were performed should also be included. Results of qualification tests on reference materials should be given for each new in-house reference material.

### 3.1 Summary information on the finished product (final lot)

Trade name: ...............................................

International non proprietary name (INN)/
Ph Eur name/
Common name of product
(whichever is appropriate): ...............................................

Batch number(s):

Finished product (final lot): ...............................................

Final bulk: ...............................................

Type of container: ...............................................

Total number of containers in this batch: ...............................................

Number of doses per container: ...............................................

Composition/volume of single human dose: ...............................................

Date of expiry: ...............................................

Date of start of period of validity: ...............................................

Storage temperature: ...............................................

Marketing authorisation number issued
by (Member state/EU): ...............................................

Name and address of manufacturer: ...............................................

Name and address of Marketing
Authorisation Holder if different: ...............................................

### 3.2 Production information

Site of manufacture: ...............................................

Date of manufacture: ...............................................

Summary information scheme on batch specific production data including dates of different production stages, different production site(s) where relevant, identification numbers and blending scheme. Indicate if a reprocessing step has taken place.

For multivalent vaccines, the attributes and tests for each strain should be included in the sections below where relevant and according to the approved marketing authorisation.

### 3.2.1 Starting materials

3.2.1.1 Cell Banks

*Full details on master and working cell banks upon first submission only (e.g certificates of analysis containing the appropriate information for the identity of the cell banks may be provided) and whenever a change has been introduced.*

Master cell bank (MCB) No and preparation date: ...............................................

Working cell bank (WCB) No and
Preparation date: ...............................................

3.2.1.2 Linear plasmid DNA

General information (batch number, date of manufacture, volume, storage temperature, storage time and approved storage period, tests (e.g. as listed below),…)

Appearance
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

DNA concentration
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Plasmid identity (if applicable)
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Poly A integrity (if applicable)
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Linearisation efficiency
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Residual Protein (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Residual DNA (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Residual RNA (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Bioburden
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Endotoxin
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

pH (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### 3.2.2 Intermediate stages

Production details, in-process controls (e.g. as listed below) and dates of tests. Identification of intermediates e.g. bulks, steps yield. Safety tests on intermediates and controls e.g. sterility, adventitious agents, special tests. Details on storage conditions…

### 3.2.2.1 mRNA

Batch N°: ................................................

Date of manufacture: ................................................

Site of manufacture: ................................................

Volume, storage temperature, storage time and approved storage period:
................................................

#### Appearance
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

#### Identity of encoded RNA
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

#### Content (RNA concentration)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

#### RNA integrity / purity
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

#### RNA impurities (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

#### 5’ Cap
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### Poly(A) tail
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### Residual DNA template
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### Residual dsRNA (if applicable)
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### Residual solvents (if applicable)
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### pH
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### Endotoxin content
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### Bioburden
Method: …………………………………………
Specification: …………………………………………
Date: …………………………………………
Result: …………………………………………

### 3.2.2.2 LNP (if applicable)

Batch N°: ................................................

Date of manufacture: ................................................

Site of manufacture: ................................................

Batch size, storage temperature, storage time and approved storage period:
................................................

Appearance
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP component identity of each
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP component content of each
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP impurities
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP size
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP polydispersity
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

pH
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Osmolality
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Residual solvents
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Endotoxin content
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Bioburden
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

### 3.2.2.3 Intermediate bulk (if applicable)

*Report results of tests for each batch of intermediate bulk used in further processing.*

Batch N°(s) of intermediate bulk: ...............................................

Date(s) of manufacture: ...............................................

Site of manufacture: ...............................................

Volume(s), batch size, storage temperature, storage time and approved storage period:
...............................................

Appearance
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

### pH

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### Identity of encoded RNA

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### Content (RNA concentration)

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### RNA encapsulation

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### RNA purity

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### RNA impurities

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### Osmolality

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

### LNP size

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP polydispersity

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

LNP component content for each

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

LNP impurities (if applicable)

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

LNP component identity for each

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Endotoxin content

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Bioburden

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

*In-vitro* expression

Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

3.2.2.4 Final bulk vaccine (if applicable)

Batch N° and volume of final bulk vaccine: ...............................................

Date of manufacture: ...............................................

Volumes, batch number (s) of all components
used during formulation, storage temperature: ...............................................

*Report dates, volumes, in process controls and results of tests for each lot, using extra pages if necessary*.

### 3.3 Batch of finished product (final lot)

Manufacturing site: ...............................................

Batch N°: ...............................................

Date of filling: ...............................................

Type of container: ...............................................

Number of containers after inspection: ...............................................

Filling volume: ...............................................

Appearance
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Appearance (visible particles)
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Appearance (sub-visible particles)
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

pH
Method: ...............................................
Specification: ...............................................
Date: ...............................................
Result: ...............................................

Osmolality

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP size
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP polydispersity
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

RNA encapsulation
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

RNA content
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP component content for each
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP impurities (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

LNP component identity for each
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Extractable volume

Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Identity of RNA encoded sequence
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

*In-vitro* expression
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

RNA integrity / purity
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

RNA impurities (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Residual solvents (if applicable)
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Endotoxin content
Method: ................................................
Specification: ................................................
Date: ................................................
Result: ................................................

Sterility test
Method: ................................................
Media: ................................................
Volume inoculated: ................................................
Date test on: ................................................
Date test off: ................................................
Result: ................................................

## 4. Certification

Certification by qualified person taking the overall responsibility for production and control of the product:

I herewith certify that _________________(name of the product) batch N°__________ was manufactured and tested according to the procedures approved by the competent authorities and complies with the quality requirements. This includes that, for any materials derived from ruminants (bovine, ovine, caprine) used in the manufacture and/or formulation of the batch of product specified above, all measures have been taken to demonstrate compliance with Directive 2001/83/EC and amending Directives 2003/63/EC and 2004/27/EC.

In addition the OMCL performing OCABR has been notified of all relevant approved variations that have an impact on product specifications or on data supplied in section 3 of this protocol as described in the EU administrative procedure for OCABR.

Name: ______________________________________________

Function: ______________________________________________

Date: ______________________________________________

Signature: ______________________________________________